A significant correlation between the number of enjoyments and the number of ages is not seen. It is thought that many of the enjoyment depend on the individual variation.

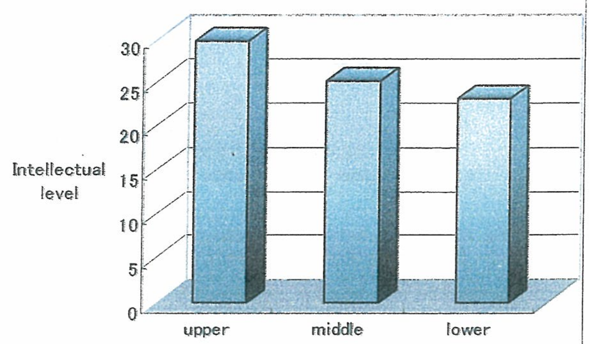

Fig. 11 Relation between the levels of enjoyment in daily life and intellectual level

Next, let's examine the stage of the enjoyment and the relation to an intellectual level.
It is understood that there is a high correlation between the enjoyment and intellectual level at free time from Figure 11. Averages of intellectual score of three groups with different number of enjoyments were compared. The score of the group with a lot of enjoyments is 29.59, the score of the group in the middle is 25.09, and the score of few groups is 23.12. It is understood to keep an intellectual higher than the person with a lot of numbers of actions at free time, score ($F=4.58$, $.01>p>.05$).

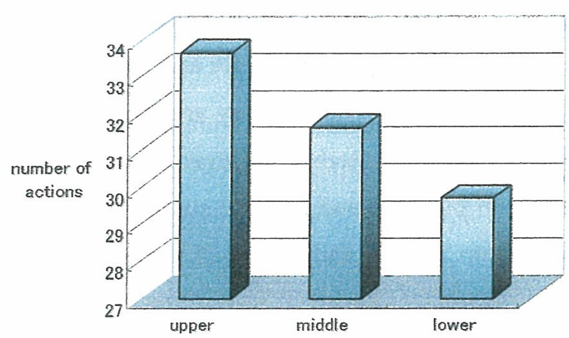

Fig. 12 Relation between the levels of enjoyment in daly life and the number of actions at free time

Next, Fig.12 shows the relation of the number of actions at free time and the degree of pleasure where it lives.

Fig.12 shows the strong correlation by the level of the number of enjoyments and pleasure where it lives. Degrees of pleasure where it lived were compared between three groups with different number of enjoyments. It is 33.64 for the group with a lot of enjoyments, 31.61 for the middle group, and 29.70 for few groups. The group with a lot of numbers of enjoyments understands and it is understood that the number of pleasure is high compared with a low group (F=10.68, p.01). In a word, it can be said that pleasure where more the enjoyment is, the more it lives is higher.

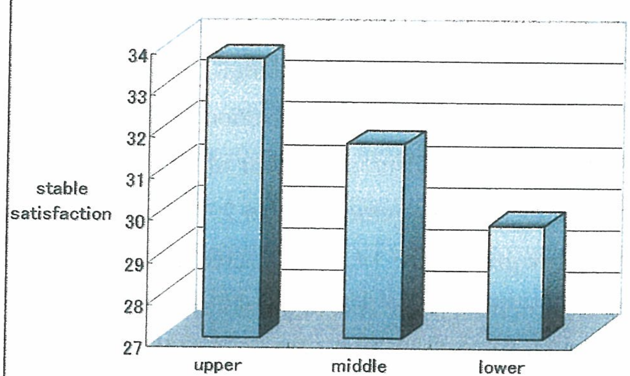

Fig. 13 Relation between the levels of enjoument in daily life and the stable satisfaction

It is Fig.13 to have shown the relation the number of enjoyments to the stability satisfaction rating.

If Fig. 13 is examined, the number of pleasure and the degree of stable satisfaction are correlated highly. Moreover, the group with a lot of pleasure has statistically higher stable satisfaction score than the middle group and the low rank group in the degree of pleasure (F=7.549 p<.01) . That is, it could be said that the degree of stable satisfactory is high, so that there is many pleasure.

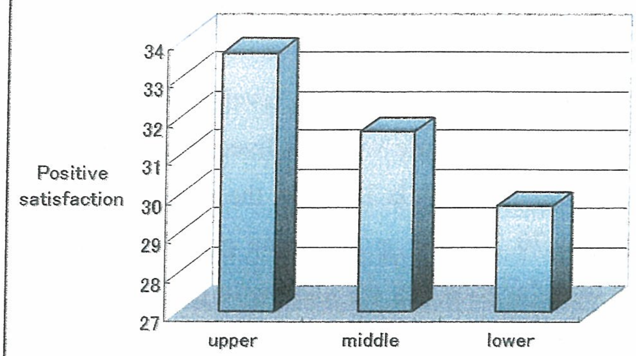

Fig. 14 Relation between the levels of enjoyment in daly life and positive satisfaction

Next, it is Fig.14 to have seen stages of the number of actions in daily life and the relations to a positive satisfaction rating.

When Fig.14 is examined, it is understood that a high correlation is seen between the level of the enjoyment and the level of a positive satisfaction rating. Mean values of three positive satisfaction rating of the group with different number of enjoyments are compared. The value of the group with a lot of numbers of enjoyments is 16.27, the value of the group in the middle is 15.00, and the values of few groups are 14.28. It decreases from a high-ranking group in order of few crowds through the middle group. It is understood that this tendency is a high statistically relation ($F=7.549$, $p<.01$). In a word, it will be able to be said more a positive satisfaction rating is the number of enjoyments, the higher. Moreover, the relation of a positive satisfaction rating to the number of enjoyments seems to be a little strong compared with a stable satisfaction rating.

There is a high correlation between the levels of the number of enjoyments and pleasure where it lives as mentioning above. Moreover, a high correlation between a number of enjoyments and a stable satisfaction rating exists. It is interpreted that the number of enjoyments relates to a positive way of life and the sense of security high.

Next, Fig.15 is an examination of the relation to the stage of the enjoyment and the amount of the social support. It is understood that the relation between the stage of the enjoyment and the amount of the social support is strongly related from Fig.15. As for amount of average of the social support, the amount of the group with a lot of numbers of enjoyments is 34.57, the amount of the middle group is 32.72, and the amounts of few groups are 30.77. When the amounts of the social support are compared between groups, it is understood that the group with a lot of numbers of enjoyments is statistically higher than the middle group and a low group (F=8.699, p<.01). In a word, it can be said more the amount of a social support is the number of enjoyments, the higher. As mentioned above, it can be interpreted that having the enjoyment a lot can keep an intellectual level high, have a high something to live for satisfaction rating, have a high stability satisfaction, have a high, positive satisfaction, and receive a lot of help from other people.

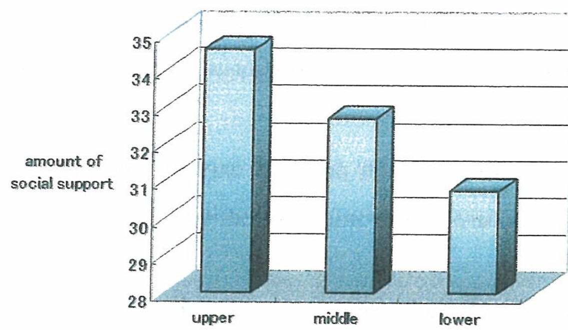

Fig. 15 Relation between the leveles of enjoyment in daily life and amount of the social support

From the above-mentioned, It has been understood that setting up a suitable target for oneself, and living positively and happily in daily life lead to the prevention of the dementia syndrome, and rise the something to live for satisfaction. It seems that it is brought close to an ideal aging so-called "Successful aging".

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研 究 成 果 一 覧 表

別紙４

研究成果の刊行に関する一覧表レイアウト（参考）

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
山田茂人	代謝、内分泌、メタボリックシンドローム	日本臨床精神薬理学会専門医制度委員会	臨床精神薬理学テキスト	星和書店	東京	2006	169-176

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Li GY, Ueki H, Kawashima T, T, Sugataka K. Muraoka T, Yamada S.	Involvement of the noradrenergic system in performancea on a continuous task requiring effortful attention.	Neuropsychobiology.	50	336-340	2004
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Involvement of the Noradrenergic System in Performance on a Continuous Task Requiring Effortful Attention

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Key Words
Saliva · 3-Methoxy-4-hydroxyphenylglycol · Uchida-Kraepelin test · Normal volunteers

Abstract
To determine the effects of noradrenergic neuronal activity on performance in continuous tasks requiring effortful attention, the performance of 23 male students in the Uchida-Kraepelin test (UKT) was examined. The UKT requires continuous arithmetic addition of single-digit figures for 25 min. The relationship of performance with saliva levels of 3-methoxy-4-hydroxyphenylglycol (sMHPG) was analyzed. Saliva samples were taken before, during and after test performance, and sMHPG levels determined by gas chromatography-mass spectrometry. There was no significant change in mean sMHPG as a result of test performance. However, when initial effort was calculated, defined as number of items completed during the 1st min subtracted from the average completed per minute in the 1st and the 2nd halves (blocks) of the test, significant correlations with sMHPG ($p = 0.0002$ for the 1st block and $p < 0.0001$ for the 2nd block) were found. Thus the data indicate that noradrenergic neuronal activity affects the performance on continuous tasks requiring effortful attention.

Introduction

Kraepelin found that performance on a serial addition test that required effortful and forced attention over a defined period showed specific time-dependent changes. The Uchida-Kraepelin test (UKT), a modification of Kraepelin's arithmetic test, and involving the continuous arithmetic addition of single-digit figures, was developed by Uchida in 1940, and has been widely used in Japan as an aptitude test to assess working ability. It is well established that initial effort and the effect of rest in the UKT are important indicators of working ability. This type of test is considered to measure the attentional capacity of the subject [1]. Although the neurochemistry underlying attention systems is not well understood, there is evidence that the catecholaminergic, cholinergic, and, indirectly, serotonergic systems are important in attentional processes [2, 3]. Coull et al. [4] have further reported evidence that the noradrenergic system is implicated in the mediation of attentional processes. Treatment of normal human volunteers with intravenous clonidine, an α_2-agonist, usually impairs performance on effortful attention tasks, an effect that is attributed to sedation resulting from the presynaptic action of the compound in down-regulating the central noradrenaline function [5]. Little, however, is known about the effects of noradrenergic neu-

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ronal activity on the performance of continuous tasks requiring effortful attention.

The plasma level of 3-methoxy-4-hydroxyphenylglycol (MHPG), a metabolite of noradrenaline, is reported to reflect noradrenergic neuronal tone in humans. Recently, it has been reported that the saliva level of MHPG correlates significantly with plasma and cerebrospinal fluid levels of MHPG, and thus may be a useful marker for detecting changes in central and peripheral catecholamine metabolism [6–9].

In the present study, in order to assess the contribution of the noradrenergic system to performance on continuous tasks with a high demand on central capacity, we investigated the relationship between performance and the level of performance on the UKT and saliva levels of MHPG (sMHPG) before, during, and after taking the UKT.

Subjects and Methods

Twenty-three male students (mean age 23.8 ± 0.7 years) were recruited. They had no psychiatric problems and did not take any anxiolytics, antidepressants, or antipsychotics. Informed consent was obtained from all participants. Physical exercise, high-monoamine diets, alcohol and caffeine were restricted before commencement of the study (>12 h before the first saliva sample).

The UKT, a test of continuous arithmetic addition of single-digit figures for 25 min, was administered using the formal methodology. The subjects are required to add each of an overlapping sequence of pairs of single-digit numbers, with the 2nd number of each pair becoming the first number of the subsequent pair. The last digit of the sum of each pair is written down by the subject in a space just below the pair. The test sheet consists of 25 lines of 115 single-digit figures in a line, so no one can complete a line in 1 min. The numbers on the test sheet are organized in such a manner that the subject changes to a new line of numbers at the signal of every minute for 15 min (1st block). They then rest for 5 min, followed by the same performance for 10 min (2nd block). The performance in each '1-min' period is measured to provide a time course for use in evaluation.

The typical results pattern in this test is that initial performance is fastest, an effect which is called 'initial effort'; the performance level then gradually decreases for around 10 min and then turns to increase during the last few min of the first 15-min block. After the 5-min interval, initial performance in the 2nd block (2nd initial effort) is again faster, compared with mean performance across the 2nd block. Thus, the time course of attentional capacity can be detected using this high-load continuous task. Performance measures on the UKT were the number of items completed in the 1st min of each block, that is the period of 1st initial effort and 2nd initial effort, and the mean number per minute completed in each block of the test. The initial effort score is the number of items completed in the 1st min of the 1st or 2nd block subtracted from the average number completed per minute in the relevant block. The effect of rest is calculated as the average task completion in 1 min on the 2nd block divided by the average task completion in 1 min on the 1st block [10].

Saliva sampling was performed concurrently with the arithmetic task, using Salivettes as described by Yamada et al. [11]. The saliva samples were taken before, during, just after, and 10 min after the test. The level of free-MHPG in the saliva at each point was measured by gas chromatography-mass spectrometry, as described by Yamada et al. [12].

Statistics

Changes in the sMHPG level with UKT performance were evaluated by one-way analysis of variance with repeated measures (4 time points). Pearson correlation coefficients were calculated to examine the relationship between sMHPG at each time point and scores on the 1st initial effort, 2nd initial effort and the effect of rest. The relationships between the different scores post-test minus pre-test values of MHPG and the indices of performances on the UKT were also calculated. The Mann-Whitney U test was used to compare the mean number of items completed in the 1st and 2nd block. A p value of <0.05 was considered significant.

Results

The mean level of MHPG in the saliva at baseline (i.e. before the test was begun) was 7.24 ± 2.58 (± SD) ng/ml, which is lower than in the previous study by Yamada et al. [12]. This discrepancy could be explained as an age-associated increase in sMHPG, in that the subjects in the earlier study were 20 years older than those in the present study. Doing the UKT had quite opposite effects on sMHPG in individual subjects; in some it increased and in others it decreased, with the result that the mean sMHPG levels were unchanged by test performance ($F(3, 66) = 0.08$, $p = 0.97$). The mean number of items completed in the 2nd block was significantly greater than in the 1st block (72.5 ± 11.9 versus 60.9 ± 13.2; $Z = 2.93$, $n = 23$, $p = 0.0029$; table 1). There was no significant correlation between saliva levels of MHPG and the number of items completed for the first 1 min or the mean number of each block (table 2). However, the first initial effort (3.6 ± 4.6) correlated significantly with baseline sMHPG ($r = 0.529$, $p = 0.0092$), and the second initial effort (9.21 ± 6.2) correlated significantly with sMHPG 10 min after the test ($r = 0.536$, $p = 0.008$; fig. 1; table 3). The mean ratio for the effect of rest was 1.18 ± 0.063, and correlated negatively with sMHPG 10 min after the test, but did not reach statistical significance ($r = -0.358$, $p = 0.09$). However, there was no significant correlation between changes in sMHPG after the test and any performances on UKT (tables 2, 3).

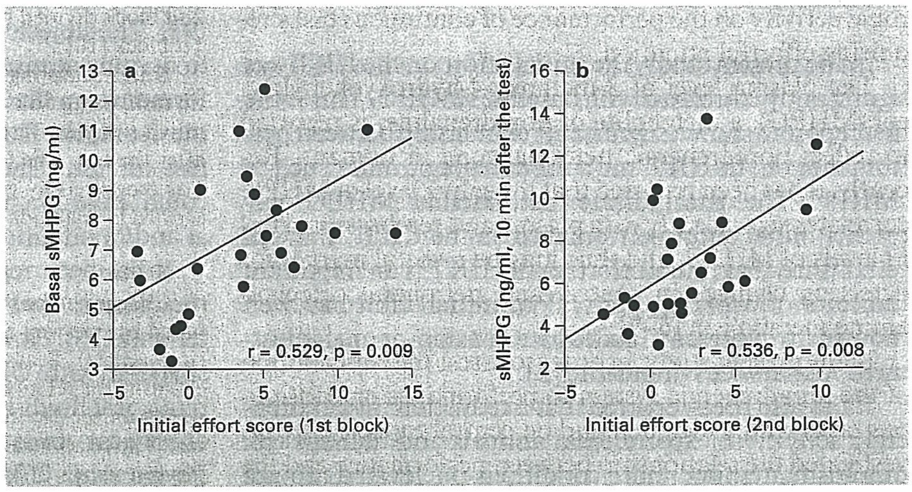

Fig. 1. Correlation between initial effort task scores and saliva MHPG. Vertical axis represents the score of first initial effort (**a**) and second initial effort (**b**). The horizontal axis represents sMHPG at baseline (**a**) and 10 min after test (**b**).

Table 1. Demographic characteristics of participants, saliva MHPG levels, and performance scores on the Uchida-Kraepelin test (means with standard deviations in parentheses)

Sex	Male
Number	23
Age, years	23.50 (0.66)
Task scores (1st block)	
First min	60.90 (13.0)
Mean for block	57.30 (10.9)
Initial effort	3.60 (4.60)
Task scores (2nd block)	
First min	76.30 (13.5)
Mean for block	67.50 (11.9)
Initial effort	9.21 (6.20)
Effect of rest	1.18 (0.066)
Saliva MHPG level, ng/ml	
Baseline (M1)	7.25 (2.37)
During rest break (M2)	7.21 (3.22)
Immediately after test (M3)	7.24 (4.16)
10 min after test (M4)	7.03 (2.79)

Table 2. Relationships of saliva MHPG levels and completed task amounts of first 1-min period or mean of each block (r values)

MHPG	M1	M2	M3	M4	M3–M1
Task scores					
First block					
First min	0.266	0.273	0.137	0.217	0.001
Mean	0.095	0.105	0.022	0.124	0.019
Second block					
First min	0.149	0.167	0.153	0.210	–0.113
Mean	0.013	0.037	–0.011	0.035	0.0001

The data represent r values of correlation coefficients. M1 = sMHPG at baseline; M2 = during rest break; M3 = immediately after test; M4 = 10 min after test; M3–M1 = MHPG values after minus values before test.

Table 3. Relationship of saliva MHPG level with initial effort scores (1st and 2nd blocks) and effect of rest scores of the Uchida-Kraepelin test (r values)

MHPG	M1	M2	M3	M4	M3–M1
1st initial effort score	0.529 (0.009)**	0.420 (0.045)*	0.333 (0.121)	0.318 (0.141)	–0.063 (0.73)
2nd initial effort score	0.277 (0.204)	0.328 (0.127)	0.461 (0.026)*	0.536 (0.008)**	–0.410 (0.052)
Effect of rest	–0.278 (0.202)	–0.291 (0.181)	–0.166 (0.453)	–0.358 (0.094)	–0.135 (0.540)

The data represent r values of correlation coefficients.
M1 = sMHPG at baseline; M2 = during rest break; M3 = immediately after test; M4 = 10 min after test; M3–M1 = MHPG values after minus MHPG values before test. p values in parentheses.
* $p < 0.05$; ** $p < 0.01$.

Discussion

In the present study, the initial effort on the UKT was significantly correlated with baseline sMHPG. This is the first report to show a significant relationship between performance on the UKT and a noradrenergic index such as sMHPG. The data indicate that baseline sMHPG may predict initial effort performance on the UKT. It is well established that initial effort on the UKT is an important indicator of working ability. Poor initial effort has been thought to represent inadequate tension or maladjustment to a new environment [13].

It has also been reported that a reduction in noradrenergic activity in experimental animals and humans can diminish attention under conditions of elevated arousal by increasing distractibility [14, 15]. Clonidine, an α_2-adrenoceptor agonist, which causes a reduction in noradrenaline neuronal activity, was found to reduce indices of attentional performance in healthy volunteers in a continuous task in which the subject has to detect target sequences of numbers [4]. Clonidine was also found to diminish the accuracy of performance in subjects with mild Parkinson's disease in a difficult attention test [16]. Finger skin blood flow was reported to be smallest during the 1st min of work on the UKT, suggesting that task concentration may be associated with the activation of sympathetic neuronal activity [17].

These findings and the present results indicate that basal noradrenergic neuronal activity may affect the time course of continuous attention under mental load stress. Especially, a high initial effort on the UKT, representing an adequate tension with normal working ability, may be sustained by the activation of noradrenergic neurons. The effect of rest inclined to negatively correlate with sMHPG. The subject with a low level of sMHPG may be slow to become accustomed to the UKT, and in this case performance on the 2nd block may be much greater than on the 1st block. This would result in a spuriously higher effect of rest. These data suggest that baseline sMHPG could serve as a noninvasive biological marker for arousal and/or attention in normal subjects.

It has been reported that UKT causes a reduction in the plasma level of homovanillic acid, a dopamine metabolite [18]. However, there was no consistent change in sMHPG with UKT performance. The MHPG level in biological fluids has been reported to increase under psychological stress and anxiety [19]. On the other hand, Peyrin et al. [20] found that prolonged submaximal work (bicycle ergometer for 1 h) under a mental load activated catecholamine systems but, in the absence of submaximal exercise, the mental load (consisting of time-limited word tests and arithmetic calculations) failed to increase urine levels of MHPG. Thus, mental load stress of the UKT variety did not, in itself, cause an increase in sMHPG. This may be because the mental task of UKT is not associated with anxiety.

The percentage of sMHPG deriving from the brain remains unknown, but sMHPG is reported to have a close correlation with MHPG in the cerebrospinal fluid [9]. Whatever the portion of sMHPG originating in the central nervous system, sMHPG could be a convenient, less invasive and useful marker for assessing noradrenergic neuronal activity in human subjects, and a useful predictive marker for performance on continuous tasks requiring effortful attention.

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Brief report

Association between the scores on the general health questionnaire-28 and the saliva levels of 3-methoxy-4-hydroxyphenylglycol in normal volunteers

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Abstract

To access the saliva level of 3-methoxy-4-hydroxy-phenylglycol (sMHPG) as an index of mental health in normal volunteers, we investigated the relationship between the sMHPG and the scores on the general health questionnaire-28 (GHQ-28). A total of 270 normal volunteers answered the GHQ-28 and the sMHPG levels were determined. The sMHPG levels in women and men were comparable. There was a significant negative correlation between the social dysfunction score on the GHQ-28 and sMHPG levels in women ($P = 0.0035$), but not in men. Moreover, the sMHPG levels also correlated with the total GHQ-28 score ($P = 0.0205$), the anxiety and the insomnia score ($P = 0.0306$) in women. These data indicate a high social dysfunction score on the GHQ-28 to be associated with a reduced noradrenergic neuronal tone thus possibly reflecting psychomotor retardation in women.

Keywords: Saliva MHPG; GHQ-28; Normal volunteers

1. Introduction

The general health questionnaire (GHQ) was edited by Goldberg (1972), and the short version (GHQ-28) has been widely used for screening psychiatric patients in the general population (Goldberg and Hillier, 1979). However, biological associations with scores on the GHQ-28 remain unclear.

3-Methoxy-4-hydroxyphenylglycol (MHPG) is a major metabolite of noradrenaline in human brain, which readily diffuses into the cerebrospinal fluid or general circulation. The plasma level of MHPG is reported to reflect noradrenergic neuronal tone in humans (Leckman et al., 1980; Yang et al., 1997). It has recently been reported that the saliva level of MHPG (sMHPG) correlates significantly with plasma and cerebrospinal fluid levels of MHPG, and thus it may be a useful marker for detecting changes in the central and peripheral catecholamine metabolism (Drebing et al., 1989; Reuster et al., 2002). Patients with anxiety disorders tend to show high plasma (Roy et al., 1986; Pliszka et al., 1988; Sevy et al., 1989) or saliva levels of MHPG (Yamada et al., 2000). In contrast, low plasma and urinary levels of MHPG have also been found in some patients with depression (Muscettola et al., 1984; Scatton et al., 1986; Carr et al., 1988; Azorin et al., 1990). We recently reported that the noradrenergic neuronal activity, as assessed by sMHPG, can predict the performance of continuous tasks requiring concentrated attention of male volunteers. A poor adaptive ability to the continuous tasks has been shown to be associated with a low level of sMHPG (Li et al., 2004). The plasma MHPG was correlated with state anxiety in healthy subjects exposed to the anticipatory stress of receiving electric shocks (Uhde et al., 1984). As a result, the MHPG levels in biological fluids may reflect some aspects of mental functioning in humans. To access the saliva level of MHPG as an index of mental health in normal volunteers, we investigated the relationship between the scores on the GHQ-28 and sMHPG levels in normal volunteers.

2. Methods

2.1. Participants

A total of 270 healthy staff members of five public offices who attend a mental health lecture were recruited. The participants included 162 men aged 45.7 ± 10.2 (range 19–67 years) and 108 women aged 41.8 ± 13.6 (range 22–59 years).

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Table 1
Correlation between each item of the GHQ-28 and MHPG saliva level in all subjects

GHQ-28 vs. sMHPG	Total ($N = 270$) z-Value (P-value)	Men ($n = 162$) z-Value (P-value)	Women ($n = 108$) z-Value (P-value)
Somatic symptoms score vs. MHPG	−1.14 (0.256)	−0.525 (0.599)	−0.925 (0.349)
Anxiety and insomnia score vs. MHPG	−1.66 (0.097)	−0.039 (0.969)	−2.16 (0.0306)*
Social dysfunction score vs. MHPG	−3.32 (0.0009)**	−1.49 (0.136)	−2.91 (0.0035)**
Severe depression score vs. MHPG	−1.99 (0.047)*	−0.56 (0.513)	−1.956 (0.0505)
Total score vs. MHPG	−1.95 (0.051)	−0.438 (0.663)	−2.30 (0.0205)*

* $P < 0.05$.
** $P < 0.01$.

2.2. Procedure

They answered GHQ-28, and thereafter saliva was collected between 13:00 and 14:00 h using a Salivette (Sarstedt, Netherlands). sMHPG was determined by gas chromatography–mass spectrometry and expressed as ng/ml as previously reported (Yamada et al., 2000). GHQ-28 consists of 28 questions about one's mental condition. Questions are rated on a four-point scale (e.g. from 'better than usual as code 1 to 'much worse than usual' as code 4). The GHQ-28 score was calculated using an original scoring method, such as codes 1 and 2 = 0, codes 3 and 4 = 1. Each question was distributed among the four items, namely, somatic symptoms, anxiety and insomnia, social dysfunction and severe depression. The data were represented for each item and the total score. This study was approved by the Institutional Review Board of Saga University Faculty of Medicine.

2.3. Data analysis

All data were analyzed using a commercially available statistical package (Stat View 4.5 Abacus Concepts Inc., USA). The gender difference of each item or the total scores of GHQ-28 was calculated by the Mann–Whitney U-test. The relationship between sMHPG, age and each item or total scores of GHQ-28 was examined using Spearman's rank order correlation after controlling for the effects of age. P values of less than 0.05 were considered to be statistically significant.

3. Results and discussion

3.1. Scores of GHQ-28 in normal volunteers

Each item score of GHQ-28 except the social dysfunction score in women was significantly higher than that in men (the somatic symptoms score, 2.17 ± 2.15 for men, 2.96 ± 2.21 for women, $P = 0.0023$; the anxiety and insomnia score, 1.74 ± 1.74 for men, 2.54 ± 2.21 for women, $P = 0.0012$; the social dysfunction score, 0.90 ± 1.36 for men, 1.19 ± 1.56 for women, not significant; the severe depression score, 0.38 ± 1.01 for men, 0.87 ± 1.56 for women, $P = 0.0054$; the total score, 5.17 ± 4.48 for men, 7.56 ± 5.74 for women, $P = 0.0004$) as observed in earlier studies (Goldberg and Hillier, 1979).

3.2. The saliva level of MHPG in normal volunteers

The sMHPG levels in women and men were comparable (11.0 ± 5.5 and 10.3 ± 5.5 ng/ml, respectively) as previously found (Yamada et al., 2000). sMHPG level was significantly correlated with age in men ($r = 0.266$, $P = 0.0008$) but not in women ($r = 0.101$, $P = 0.30$). This gender difference may be explained by a variation of MHPG with the menstrual phase in women (Odink et al., 1990).

3.3. A correlation between sMHPG and the scores of GHQ-28

As shown in Table 1, the sMHPG levels after controlling for the effects of age were significantly correlated with the social dysfunction score ($z = -2.91$, $P = 0.0035$), the total GHQ-28 score ($z = -2.30$, $P = 0.0205$) and the anxiety and insomnia score ($z = -2.16$, $P = 0.0306$) in women. On the other hand, there was no correlation between the sMHPG and any item of GHQ-28 in men (Table 1). The data indicated that a high score of social dysfunction on the GHQ-28 was associated with a reduced noradrenergic neuronal tone. The social dysfunction score of the GHQ-28 consists of seven questions, which measure a state of psychomotor retardation. This is the first report showing a significant correlation between scores on GHQ-28 and MHPG in the general female population.

As shown in Table 1, a negative association between sMHPG and scores on GHQ-28 was found in women, but not in men. The mechanism underlying the gender difference was unclear. A gender difference in stress-induced changes in noradrenaline levels and/or cortisol levels in biological fluids has been reported (Forsman and Lundberg, 1982). Estrogen has been shown to modulate both MHPG and mood in humans (Best et al., 1992; Del Rio et al., 1994). sMHPG levels in male psychiatric outpatients with anxiety disorders at their initial consultation were two times higher than those in male volunteers, but the sMHPG levels in young female patients with anxiety disorders has been reported to be the same as those in female volunteers (Yamada et al., 2000). These data indicate that estrogen was associated with a reduction of the noradrenergic neuronal activity in response to mental stress that may, at least partially, explain the gender difference regarding the correlation between the sMHPG level and the GHQ-28 score.

The present study revealed poor mental health as assessed by GHQ-28 to be associated with a low sMHPG in women. Overall, these data indicate that a high score on the GHQ-28, especially a high social dysfunction score, is thus associated with a reduced noradrenergic neuronal tone in women.

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九州神経精神医学雑誌　印刷中

在宅高齢者の「かなひろいテスト」成績の経時変化

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過去８年間に老人健康教室に参加し「かなひろいテスト」（KANA）と Mini Mental State Examination (MMSE)を経時的に評価されている 65 歳以上の在宅高齢者 507 名を対象に、両テストの認知症のスクリーニング法としての有用性を検討した。初回に測定した KANA 得点と MMSE 得点には有意な正の相関が認められた　(r=0.44, P<0.0001, n=314)。また過去 10 年間に４回以上 KANA を施行された 73 名と MMSE を施行された８名についてテスト成績の経時的変化を検討すると KANA の成績は初回と比べて３回目と４回目の時点で有意な改善が認められた（F(3,74)=22.5,P<0.001）。一方、MMSE 得点は初回に比べ有意ではないが漸次減少していた。以上の結果から KANA は初回施行におけるスクリーニング法として有用であるが、3 回以上繰り返すと学習効果が認められ知的機能の経時的な変化の評価には不適当であることが示唆された。

<はじめに>

来るべき超高齢化社会に向けて、認知症予防の取り組みが各地で行われている。認知機能の評価には一般に Mini Mental State Examination　(MMSE）や長谷川式スケールが用いられているが、対面質問形式で行われるため被験者の精神的負担も大きく、多人数を対象としたスクリーニングには不向きである。そこで認知症の一次スクリーニングのための様々なテストバッテリーが検討されている 7)。その中で金子が開発したカナひろいテスト（KANA）は全て平仮名で書かれている昔話の筋を追いながら、「あいうえお」の文字を拾い上げていくという課題であり、被験者の施行に対する抵抗も少なく、2 分間で集団を対象に作業記憶の程度を評価出来る点で認知症のスクリーニングテストとして注目されている検査である 4）,5）,6)。これまでの高齢者を対象とした KANA を用いた研究では積極的な日常生活習慣を持つ人が高得点を示すという研究や 10)、パーキンソン病患者の P300 潜時と KANA 得点に有意な相関を認めた研究 2）などがある。一方、執筆に関係した

趣味を持つ事や高学歴で高得点となるが、Kohs 立方組み合わせテストのほうが前痴呆状態を判別するのに有用であるという報告 12) もあり、KANA の有用性についての評価はさだまっていない。また繰り返し施行した場合の学習効果についての検討がなされていない。

平成 2 年より K 町の有志によって同町在住の 65 歳以上の高齢者を対象に KANA および MMSE による知的機能検査と MRI による脳形態の関連に関する研究が開始された。その後、知的機能の低下の実態の把握とその予防のための地域の支援システムを作る試みがなされてきた。初期の検討で初回測定の KANA の成績と MMSE の成績に高い相関が認められたことから 8) 現在は毎月 1 回各地区持ち回りで高齢者健康教室を開催し、健康に関する講演が行われ参加者全員に KANA を、希望者に MMSE を施行している。毎年 65 歳以上の地区住民の約 7 割に KANA が施行され、その得点が 60 歳代で 10 点以下、70 歳代で 9 点以下、80 歳代で 8 点以下の要注意者は 2 次スクリーニングとして保健師が家庭訪問を行い MMSE が施行されている。その中で MMSE 得点が 20 点以下の場合にかかりつけ医または協力医療機関に紹介するとともに、継続訪問を行い健康状態や生活状況の把握、家族への助言、介護者の健康管理などが行われている。本研究ではこれまで蓄積された KANA および MMSE のデーターから繰り返し施行によるテスト成績の経時的変動について検討した。

＜対象および方法＞

K 町在住の 65 歳以上の在宅高齢者を対象に脳検診の希望を募った。平成 6 年の脳検診の参加者は述べ 506 名（男性　159 名、女性　347 名、平均年齢 74.1 歳）であった。そのうち MMSE と KANA を施行された 314 名を解析の対象とした。

かなひろいテスト（KANA）: KANA はすべてひらがなで書かれた昔話の内容を理解しながら読み進めて行くと同時に文中に出てくる「あいうえお」の文字に制限時間 2 分間でマークしていくもので、全部正解すると 56 点になる。

KANA の成績と MMSE の成績の経時変化 : KANA の成績と MMSE の成績の変動を縦断的に検討するために、KANA 及び MMSE を 8 年間に 4 回以上施行された参加者を対象とした。すなわち、同一人物について、初年度、1-2 年後、3-4 年後、5-8 年後の時点の KANA 及び MMSE の成績について、反復測定分散分析を行い、成績の変動を調べた。また 8 年間に 2 回以上 KANA および MMSE をうけた 334 名を対象とし、初年度、1-2 年後、3-4 年後、5-8 年後の KANA 及び MMSE の成績の変動を一元配置分散分析で調べた。

KANA と MMSE の関連 : 初回測定の KANA の成績と MMSE の成績に有意な相関があることは先行研究で明らかにしているが 7)、今回は両テスト成績の相関の経時変を Pearson の相関係数を用いて検討した。$P<0.05$ を有意とした。

尚、病床にあるもの、認知症の診断を受けているものは除外した。本研究は佐賀大学医学部倫理委員会の承認を得ている。

＜結果＞

これまで KANA は毎年 1 回施行されてきたが、最近 8 年間にテストをうけた被験者は 474 名（男性　159 名、女性　347 名；平均年齢 73.9±6.2 歳）であり、そのうち 313 名が MMSE

も同時に施行された。測定初年度のKANAの得点は　15.8±9.7、MMSEの得点は24.9±3.8　であった。年齢と初回の KANA 及び MMSE の成績の間には有意な相関があった（KANA r=-0.422、P<0.0001, MMSE r=-0.387, P<0.0001, n=314）。最近 8 年間にKANAを4回以上受けた被験者は73名であった。個人のKANAの成績の経時変化をTable 1 に示す。KANA は初回に比べて、3回目と4回目の時点で有意な点数の上昇が認められた（F(3,74)=23.9,P<0.0001）。この成績の改善に男女差は認められなかった。一方 MMSE を 8 年間で 4 回以上受けたものは 8 名であり 4 回の間に有意な変動は認められなかった（F(3,7)=1.28, P=0.30）。そこで8年間に2回ないし3回MMSEを施行した参加者を含め、延べの成績でみると初回が24.9±3.8点(N=314)、2-3年後の2回目が24.9±4.1(N=113)、4-5年後の3回目が 23.8±4.1 点（N=49)、6-8 年後の 4 回目が 23.6±4.1 点（N=34)であり、この4群間には有意差は認めなかった。また初年度と2回目の同一個人のKANA及びMMSEの成績には有意な正の相関が認められた（初回 r=0.44,P<0.0001, n=314；2回目 r＝0.38、P<0.0001）が3回目と4回目のKANA と MMSEには相関は認めなかった（3回目　r=0.11, P=0.46, n=46; 4回目 r=0.45,P=0.23, n=10)。

Table 1, 同一個人のKANAおよびMMSE成績の経時変化

	初年度	2～3年後	4～5年後	6～8年後	
KANA (n=75)	15.8±9.7	14.03±6.7	17.9±9.1*	22.9±10.5**	F(3,74)=23.9 P<0.0001
MMSE (n=8)	22.4±3.0	22.1±3.8	20.75±3.7	20.5±4.6	F(3,7)=1.28, P=0.30

Table 2, KANA及びMMSE成績の経時変化と両者の相関　(2回以上施行)

	初年度	2～3年後	4～5年後	6～8年後	
KANA	14.1±9.6	15.1±9.3*	18.6±10.4**	22.1±10.7**	F(3,1122)=23.2
N	475	352	222	77	P<0.0001
MMSE	25.0±3.8	25.1±4.1	23.6±4.1	23.6±4.1	F(3,513)=3.03
N	333	113	49	34	P=0.029
相関 r (n)	0.44 (314)	0.38 (108)	0.11 (46)	0.44 (10)	
	P<0.0001	P<0.0001	P=0.46	P=0.23	